

KAPLAN & SADOCK'S

SYNOPSIS OF PSYCHIATRY

Behavioral Sciences/Clinical Psychiatry

TENTH EDITION



BENJAMIN JAMES SADOCK, M.D.

VIRGINIA ALCOTT SADOCK, M.D.



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Psychiatry

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Table 10.3-4
Criteria for Clinical Diagnosis of HIV Type 1-Associated Dementia Complex

Laboratory evidence for systemic human immunodeficiency virus (HIV) type 1 infection with confirmation by Western blot, polymerase chain reaction, or culture.

Acquired abnormality in at least two of cognitive abilities for a period of at least 1 month: attention and concentration, speed of processing information, abstraction and reasoning, visuospatial skills, memory and learning, and speech and language. The decline should be verified by reliable history and mental status examination. History should be obtained from an informant, and examination should be supplemented by neuropsychological testing.

Cognitive dysfunction causes impairment in social or occupational functioning. Impairment should not be attributable solely to severe systemic illness.

At least one of the following:

Acquired abnormality in motor function verified by clinical examination (e.g., slowed rapid movements, abnormal gait, incoordination, hyperreflexia, hypertonía, or weakness), neuropsychological tests (e.g., fine motor speed, manual dexterity, or perceptual motor skills), or both.

Decline in motivation or emotional control or a change in social behavior. This may be characterized by a change in personality with apathy, inertia, irritability, emotional lability, or a new onset of impaired judgment or disinhibition.

This does not exclusively occur in the context of a delirium. Evidence of another etiology, including active central nervous system opportunistic infection, malignancy, psychiatric disorders (e.g., major depression), or substance abuse, if present, is not the cause of the previously mentioned symptoms and signs.

(Adapted from Working Group of the American Academy of Neurology AIDS Task Force: Nomenclature and research case definitions for neurologic manifestations of human immunodeficiency virus-type 1 (HIV-1) infection. *Neurology*. 1991;41:778-785, with permission.)

Inasmuch as memory is important for orientation to person, place, and time, orientation can be progressively affected during the course of a dementing illness. For example, patients with dementia may forget how to get back to their rooms after going to the bathroom. No matter how severe the disorientation seems, however, patients show no impairment in their level of consciousness.

Dementing processes that affect the cortex, primarily dementia of the Alzheimer's type and vascular dementia, can affect patients' language abilities. DSM-IV-TR includes aphasia as one of the diagnostic criteria. The language difficulty may be characterized by a vague, stereotyped, imprecise, or circumstantial locution, and patients may also have difficulty naming objects.

Psychiatric and Neurological Changes

Personality. Changes in the personality of a person with dementia are especially disturbing for their families. Preexisting personality traits may be accentuated during the development of a dementia. Patients with dementia may also become introverted and seem to be less concerned than they previously were about the effects of their behavior on others. Persons with dementia who have paranoid delusions are generally hostile to family members and caretakers. Patients with frontal and temporal involvement are likely to have marked personality changes and may be irritable and explosive.



Table 10.3-5
DSM-IV-TR Diagnostic Criteria for Dementia of the Alzheimer's Type

- A. The development of multiple cognitive deficits manifested by both
 - (1) memory impairment (impaired ability to learn new information or to recall previously learned information)
 - (2) one (or more) of the following cognitive disturbances:
 - (a) aphasia (language disturbance)
 - (b) apraxia (impaired ability to carry out motor activities despite intact motor function)
 - (c) agnosia (failure to recognize or identify objects despite intact sensory function)
 - (d) disturbance in executive functioning (i.e., planning, organizing, sequencing, abstracting)
 - B. The cognitive deficits in Criteria A1 and A2 each cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning.
 - C. The course is characterized by gradual onset and continuing cognitive decline.
 - D. The cognitive deficits in Criteria A1 and A2 are not due to any of the following:
 - (1) other central nervous system conditions that cause progressive deficits in memory and cognition (e.g., cerebrovascular disease, Parkinson's disease, Huntington's disease, subdural hematoma, normal-pressure hydrocephalus, brain tumor)
 - (2) systemic conditions that are known to cause dementia (e.g., hypothyroidism, vitamin B₁₂ or folic acid deficiency, niacin deficiency, hypercalcemia, neurosyphilis, HIV infection)
 - (3) substance-induced conditions
 - E. The deficits do not occur exclusively during the course of a delirium.
 - F. The disturbance is not better accounted for by another Axis I disorder (e.g., major depressive disorder, schizophrenia).
- Code based on presence or absence of a clinically significant behavioral disturbance:
- Without behavioral disturbance:** if the cognitive disturbance is not accompanied by any clinically significant behavioral disturbance.
- With behavioral disturbance:** if the cognitive disturbance is accompanied by a clinically significant behavioral disturbance (e.g., wandering, agitation).
- Specify subtype:**
- With early onset:** if onset is at age 65 years or below
- With late onset:** if onset is after age 65 years
- Coding note:** Also code Alzheimer's disease on Axis III. Indicate other prominent clinical features related to the Alzheimer's disease on Axis I (e.g., Mood disorder due to Alzheimer's disease, with depressive features, and Personality change due to Alzheimer's disease, aggressive type).

(From American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Text rev. Washington, DC: American Psychiatric Association; copyright 2000, with permission.)

Hallucinations and Delusions. An estimated 20 to 30 percent of patients with dementia (primarily patients with dementia of the Alzheimer's type) have hallucinations, and 30 to 40 percent have delusions, primarily of a paranoid or persecutory and unsystematized nature, although complex, sustained, and well-systematized delusions are also reported by these patients. Physical aggression and other forms of violence are common in demented patients who also have psychotic symptoms.



Table 16.1-1

Key Phenomenological Features of Major Anxiety Disorders As Defined by DSM-IV-TR

Panic disorder

Recurrent unexpected panic attacks characterized by four or more of the following:

- Palpitations
- Sweating
- Trembling or shaking
- Shortness of breath
- Feeling of choking (also known as *air hunger*)
- Chest pain or discomfort
- Nausea or abdominal distress
- Feeling dizzy, lightheaded, or faint
- Depersonalization or derealization
- Fear of losing control or going crazy
- Fear of dying
- Numbness or tingling
- Chills or hot flashes

Persistent concern of future attacks

Worry about the meaning of or consequences of the attacks (e.g., heart attack or stroke)

Significant change in behavior related to the attacks (e.g., avoiding places at which panic attacks have occurred)

± Presence of agoraphobia

Agoraphobia

Fear of being in places or situations from which escape might be difficult, embarrassing, or in which help may be unavailable in the event of having a panic attack

Often results in avoidance of the feared places or situations, for example:

- Crowds
- Stores
- Bridges
- Tunnels
- Traveling on a bus, train, or airplane
- Theaters
- Standing in a line
- Small enclosed rooms

Social phobia

Marked and persistent fear of one or more social or performance situations in which the person is concerned about negative evaluation or scrutiny by others, for example:

- Public speaking
- Writing, eating, or drinking in public
- Initiating or maintaining conversations

Fears humiliation or embarrassment, perhaps by manifesting anxiety symptoms (e.g., blushing or sweating)

Feared social or performance situations are avoided or endured with intense anxiety or distress

Specific phobia

Marked and persistent fear that is excessive, unreasonable, cued by the presence or anticipation of a specific object or situation, for example:

- Flying
- Enclosed spaces
- Heights
- Storms
- Animals (e.g., snakes or spiders)
- Receiving an injection
- Blood

Provokes an immediate anxiety response

Recognition that the fear is excessive or unreasonable

Avoidance, anticipatory anxiety, or distress is significantly impairing

Obsessive-compulsive disorder

Has obsessions or compulsions

Obsessions are defined as recurrent and persistent thoughts, impulses, or images that are experienced as intrusive and inappropriate, for example:

- Contamination
- Repeated doubts
- Order
- Impulses
- Sexual images

Compulsions are defined as repetitive behaviors or mental acts whose goal is to prevent or to reduce anxiety or distress, for example:

- Hand washing
- Ordering
- Checking
- Praying
- Counting
- Repeating words

Recognition that the fear is excessive or unreasonable

Obsessions cause marked distress, are time-consuming (more than 1 hour per day), or cause significant impairment in social, occupational or other daily functioning

Generalized anxiety disorder or overanxious disorder

Excessive anxiety and worry about a number of events or activities (future oriented), occurring more days than not for at least 6 months

Worry is difficult to control

Worry is associated with at least three of the following symptoms:

- Restlessness or feeling keyed up or on edge
- Easily fatigued
- Difficulty concentrating
- Irritability
- Muscle tension
- Sleep disturbance

Anxiety and worry cause significant distress and impairment in social, occupational, or other daily functioning

Separation anxiety disorder

Developmentally inappropriate and excessive anxiety

concerning separation from home or to an attachment figure. Characterized by three or more of the following:

Recurrent and excessive distress when separation from home or major attachment figure occurs or is anticipated

Persistent and excessive worry that major attachment figure will be lost or harmed

Persistent and excessive worry that an event will lead to separation from major attachment figure (e.g., getting kidnapped)

Persistent and recurring fear of being alone or without attachment figure at home

Reluctance or refusal to sleep away from home or without being near major attachment figure

Duration of at least 4 weeks

Age of onset before 18 years of age

Causes distress or impairment in functioning

Physical symptoms (e.g., headaches, stomachaches, nausea, and vomiting) when separation occurs or is anticipated

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Table 16.1-3

ICD-10 Diagnostic Criteria for Phobic Anxiety Disorders

Agoraphobia

- A. There is marked and consistently manifest fear in, or avoidance of, at least two of the following situations:
- (1) crowds;
 - (2) public places;
 - (3) traveling alone;
 - (4) traveling away from home.
- B. At least two symptoms of anxiety in the feared situation must have been present together, on at least one occasion since the onset of the disorder, and one of the symptoms must have been from items (1) to (4) listed below.

Autonomic arousal symptoms

- (1) palpitations or pounding heart, or accelerated heart rate;
- (2) sweating;
- (3) trembling or shaking;
- (4) dry mouth (not due to medication or dehydration);

Symptoms involving chest and abdomen

- (5) difficulty in breathing;
- (6) feeling of choking;
- (7) chest pain or discomfort;
- (8) nausea or abdominal distress (e.g., churning in stomach);

Symptoms involving mental state

- (9) feeling dizzy, unsteady, faint, or light-headed;
- (10) feelings that objects are unreal (derealization), or that the self is distant or "not really here" (depersonalization);
- (11) fear of losing control, "going crazy," or passing out;
- (12) fear of dying

General symptoms

- (13) hot flushes or cold chills;
- (14) numbness or tingling sensations.

- C. Significant emotional distress is caused by the avoidance or by the anxiety symptoms, and the individual recognizes that these are excessive or unreasonable.
- D. Symptoms are restricted to, or predominate in, the feared situations or contemplation of the feared situations.
- E. *Most commonly used exclusion clause.* Fear or avoidance of situations (Criterion A) is not the result of delusions, hallucinations, or other disorders such as organic mental disorders, schizophrenia and related disorders, mood [affective] disorders, or obsessive-compulsive disorder, and is not secondary to cultural beliefs.

The presence or absence of panic disorder in a majority of agoraphobic situations may be specified by using a fifth character.

Without panic disorder**With panic disorder****Options for rating severity**

Severity in agoraphobia may be rated by indicating the degree of avoidance, taking into account the specific cultural setting. Severity in social phobias may be rated by counting the number of panic attacks.

Social phobias

- A. Either of the following must be present.

- (1) marked fear of being the focus of attention, or fear of behaving in a way that will be embarrassing or humiliating;
- (2) marked avoidance of being the focus of attention, or of situations in which there is fear of behaving in an embarrassing or humiliating way.

These fears are manifested in social situations, such as eating or speaking in public, encountering known individuals in public or entering or enduring small group situations (e.g., parties, meetings, classrooms).

- B. At least two symptoms of anxiety in the feared situation as defined in agoraphobia, Criterion B, must have been manifest at some time since the onset of the disorder, together with at least one of the following symptoms:

- (1) blushing or shaking;
- (2) fear of vomiting;
- (3) urgency or fear of micturition or defecation.

- C. Significant emotional distress is caused by the symptoms or by the avoidance, and the individual recognizes that these are excessive or unreasonable.

- D. Symptoms are restricted to, or predominate in, the feared situations or contemplation of the feared situations.

- E. *Most commonly used exclusion clause.* The symptoms listed in Criteria A and B are not the result of delusions, hallucinations, or other disorders such as organic mental disorders, schizophrenia and related disorders, mood [affective] disorders, or obsessive-compulsive disorder, and are not secondary to cultural beliefs.

Specific (isolated) phobias.

- A. Either of the following must be present:

- (1) marked fear of a specific object or situation not included in agoraphobia or social phobia;
- (2) marked avoidance of a specific object or situation not included in agoraphobia or social phobia.

Among the most common objects and situations are animals, birds, insects, heights, thunder, flying, small enclosed spaces the sight of blood or injury, injections, dentists, and hospitals.

- B. Symptoms of anxiety in the feared situation as defined in agoraphobia, Criterion B, must have been manifest at some time since the onset of the disorder.

- C. Significant emotional distress is caused by the symptoms or by the avoidance, and the individual recognizes that these are excessive or unreasonable.

- D. Symptoms are restricted to the feared situation or contemplation of the feared situation.

If desired, the specific phobias may be subdivided as follows.

- animal type (e.g., insects, dogs)
- nature-forces type (e.g., storms, water)
- blood, injection, and injury type.
- situation type (e.g., elevators, tunnels)
- other type

Other phobic anxiety disorders**Phobic anxiety disorder, unspecified**

Table 16.1-4

ICD-10 Diagnostic Criteria for Other Anxiety Disorders

Panic disorder [episodic paroxysmal anxiety]

A. The individual experiences recurrent panic attacks that are not consistently associated with a specific situation or object and that often occur spontaneously (i.e., the episodes are unpredictable). The panic attacks are not associated with marked exertion or with exposure to dangerous or life-threatening situations.

B. A panic attack is characterized by all of the following:

- (1) it is a discrete episode of intense fear or discomfort;
- (2) it starts abruptly;
- (3) it reaches a maximum within a few minutes and lasts at least some minutes;
- (4) at least four of the symptoms listed below must be present, one of which must be from items (a) to (d):

Autonomic arousal symptoms

- (a) palpitations or pounding heart, or accelerated heart rate;
- (b) sweating;
- (c) trembling or shaking;
- (d) dry mouth (not due to medication or dehydration);

Symptoms involving chest and abdomen

- (e) difficulty in breathing;
- (f) feeling of choking;
- (g) chest pain or discomfort;
- (h) nausea or abdominal distress (e.g., churning in stomach);

Symptoms involving mental state

- (i) feeling dizzy, unsteady, faint, or light-headed;
- (j) feeling that objects are unreal (derealization), or that the self is distant or "not really here" (depersonalization);
- (k) fear of losing control, "going crazy," or passing out;
- (l) fear of dying;

General symptoms

- (m) hot flushes or cold chills;
- (n) numbness or tingling sensations.

C. *Most commonly used exclusion clause.* Panic attacks are not due to a physical disorder, organic mental disorder, or other mental disorders, such as schizophrenia and related disorders, mood [affective] disorders, or somatoform disorders.

The range of individual variation in both content and severity is so great that two grades, moderate and severe, may be specified, if desired, with a fifth character.

Panic disorder, moderate

At least four panic attacks in a 4-week period.

Panic disorder, severe

At least four panic attacks per week over a 4-week period.

Generalized anxiety disorder

Note. In children and adolescents the range of complaints by which the general anxiety is manifest is often more limited than in adults, and the specific symptoms of autonomic arousal are often less prominent. For these individuals, an alternative set of criteria is provided for use (in generalized anxiety disorder of childhood) if preferred.

A. There must have been a period of at least 6 months with prominent tension, worry, and feelings of apprehension about everyday events and problems.

B. At least four of the symptoms listed below must be present, at least one of which must be from items (1) to (4):

Autonomic arousal symptoms

- (1) palpitations or pounding heart, or accelerated heart rate;
- (2) sweating;
- (3) trembling or shaking;
- (4) dry mouth (not due to medication or dehydration);

Symptoms involving chest and abdomen

- (5) difficulty in breathing;
- (6) feeling of choking;
- (7) chest pain or discomfort;
- (8) nausea or abdominal distress (e.g., churning in stomach);

Symptoms involving mental state

- (9) feeling dizzy, unsteady, faint, or light-headed;
- (10) feelings that objects are unreal (derealization), or that the self is distant or "not really here" (depersonalization);
- (11) fear of losing control, "going crazy," or passing out;
- (12) fear of dying;

General symptoms

- (13) hot flushes or cold chills;
- (14) numbness or tingling sensations;

Symptoms of tension

- (15) muscle tension or aches and pains;
- (16) restlessness and inability to relax;
- (17) feeling keyed up, on edge, or mentally tense;
- (18) a sensation of a lump in the throat, or difficulty in swallowing;

Other nonspecific symptoms

- (19) exaggerated response to minor surprise or being startled;
- (20) difficulty in concentrating, or mind "going blank," because of worrying or anxiety;
- (21) persistent irritability;
- (22) difficulty in getting to sleep because of worrying.

C. The disorder does not meet the criteria for panic disorder, phobic anxiety disorders, obsessive-compulsive disorder, or hypochondriacal disorder.

D. *Most commonly used exclusion clause.* The anxiety disorder is not due to a physical disorder, such as hyperthyroidism, an organic mental disorder, or a psychoactive substance-related disorder, such as excess consumption of amphetaminelike substances or withdrawal from benzodiazepines.

Mixed anxiety and depressive disorder

There are so many possible combinations of comparatively mild symptoms for these disorders that specific criteria are not given other than those already in *Clinical Descriptions and Diagnostic Guidelines*. It is suggested that researchers wishing to study patients with these disorders should arrive at their own criteria within the guidelines, depending upon the setting and purpose of their studies.

Other mixed anxiety disorders**Other specified anxiety disorders****Anxiety disorder, unspecified**

abnormal findings in the right hemisphere but not the left hemisphere; this finding suggests that some types of cerebral asymmetries may be important in the development of anxiety disorder symptoms in specific patients. Functional brain-imaging (fMRI) studies—for example, positron emission tomography (PET), single photon emission computed tomography (SPECT), and electroencephalography (EEG)—of patients with anxiety disorder have variously reported abnormalities in the frontal cortex, the occipital and temporal areas, and, in a study of panic disorder, the parahippocampal gyrus. Several functional neuroimaging studies have implicated the caudate nucleus in the pathophysiology of OCD. In posttraumatic stress disorder, fMRI studies have found increased activity in the amygdala, a brain region associated with fear (see Color Plate Fig. 16.1–1 on p. 494). A conservative interpretation of these data is that some patients with anxiety disorders have a demonstrable functional cerebral pathological condition and that the condition may be causally relevant to their anxiety disorder symptoms.

Genetic Studies. Genetic studies have produced solid evidence that at least some genetic component contributes to the development of anxiety disorders. Heredity has been recognized as a predisposing factor in the development of anxiety disorders. Almost half of all patients with panic disorder have at least one affected relative. The figures for other anxiety disorders, although not as high, also indicate a higher frequency of the illness in first-degree relatives of affected patients than in the relatives of nonaffected persons. Although adoption studies with anxiety disorders have not been reported, data from twin registers also support the hypothesis that anxiety disorders are at least partially genetically determined. Clearly, a linkage exists between genetics and anxiety disorders, but no anxiety disorder is likely to result from a simple mendelian abnormality. One report has attributed about 4 percent of the intrinsic variability of anxiety within the general population to a polymorphic variant of the gene for the serotonin transporter, which is the site of action of many serotonergic drugs. Persons with the variant produce less transporter and have higher levels of anxiety.

In 2005, a scientific team, led by National Institute of Mental Health (NIMH) grantee and Noble Laureate Dr. Eric Kandel demonstrated that knocking out a gene in the brain's fear hub creates mice unperturbed by situations that would normally trigger instinctive or learned fear responses. The gene codes for *stathmin*, a protein that is critical for the amygdala to form fear memories. Stathmin knockout mice showed less anxiety when they heard a tone that had previously been associated with a shock, indicating less learned fear. The knockout mice also were more susceptible to explore novel open space and maze environments, a reflection of less innate fear. Kandel suggests that stathmin knockout mice can be used as a model of anxiety states of mental disorders with innate and learned fear components: these animals could be used to develop new anti-anxiety agents. Whether stathmin is similarly expressed and pivotal for anxiety in the human amygdala remains to be confirmed.

Neuroanatomical Considerations. The locus ceruleus and the raphe nuclei project primarily to the limbic system and the cerebral cortex. In combination with the data from brain-imaging studies, these areas have become the focus of much hypothesis-forming about the neuroanatomical substrates of anxiety disorders.

LIMBIC SYSTEM. In addition to receiving noradrenergic and serotonergic innervation, the limbic system also contains a high concentration of GABA_A receptors. Ablation and stimulation studies in nonhuman primates have also implicated the limbic system in the generation of anxiety and fear responses. Two areas of the limbic system have received special attention in the literature: increased activity in the septohippocampal pathway, which may lead to anxiety, and the cingulate gyrus, which has been implicated particularly in the pathophysiology of OCD.

CEREBRAL CORTEX. The frontal cerebral cortex is connected with the parahippocampal region, the cingulate gyrus, and the hypothalamus and, thus, may be involved in the production of anxiety disorders. The temporal cortex has also been implicated as a pathophysiological site in anxiety disorders. This association is based in part on the similarity in clinical presentation and electrophysiology between some patients with temporal lobe epilepsy and patients with OCD.

ICD-10

In the 10th revision of *International Statistical Classification of Diseases and Related Health Problems* (ICD-10), neurotic (anxiety) disorders are grouped with stress-related and somatoform disorders because of "their historical association with the concept of neurosis and the association of a substantial (although uncertain) proportion of these disorders with psychological causation." In ICD-10, mixtures of symptoms are described

Table 16.1–5
ICD-10 Diagnostic Criteria for
Obsessive-Compulsive Disorder

- A. Either obsessions or compulsions (or both) are present on most days for a period of at least 2 weeks.
- B. Obsessions (thoughts, ideas, or images) and compulsions (acts) share the following features, all of which must be present:
 - (1) They are acknowledged as originating in the mind of the patient and are not imposed by outside persons or influences.
 - (2) They are repetitive and unpleasant, and at least one obsession or compulsion that is acknowledged as excessive or unreasonable must be present.
 - (3) The patient tries to resist them (but resistance to very long-standing obsessions or compulsions may be minimal). At least one obsession or compulsion that is unsuccessfully resisted must be present.
 - (4) Experiencing the obsessive thought or carrying out the compulsive act is not in itself pleasurable. (This should be distinguished from the temporary relief of tension or anxiety.)
- C. The obsessions or compulsions cause distress or interfere with the patient's social or individual functioning, usually by wasting time.
- D. *Most commonly used exclusion clause.* The obsessions or compulsions are not the result of other mental disorders, such as schizophrenia and related disorders or mood [affective] disorders.

The diagnosis may be further specified by the following four-character codes:

- Predominantly obsessional thoughts and ruminations
- Predominantly compulsive acts (obsessional rituals)
- Mixed obsessional thoughts and acts
- Other obsessive-compulsive disorders
- Obsessive-compulsive disorder, unspecified

(From World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research*. Copyright, World Health Organization, Geneva, 1993, with permission.)

Table 16.1–6
ICD-10 Diagnostic Criteria for Reactions
to Severe Stress

Acute stress reaction

- A. The patient must have been exposed to an exceptional mental or physical stressor.
- B. Exposure to the stressor is followed by an immediate onset of symptoms (within 1 hour).
- C. Two groups of symptoms are given: the acute stress reaction is graded as:
Mild
Only Criterion (1) below is fulfilled.
Moderate
Criterion (1) is met, and there are any two symptoms from Criterion (2).
Severe
Either criterion (1) is met, and there are any four symptoms from criterion (2); or there is dissociative stupor.
(1) Criteria B, C, and D for generalized anxiety disorder are met.
(2) (a) Withdrawal from expected social interaction.
(b) Narrowing of attention
(c) Apparent disorientation
(d) Anger or verbal aggression
(e) Despair or hopelessness
(f) Inappropriate or purposeless overactivity
(g) Uncontrollable and excessive grief (judged by local cultural standards).
- D. If the stressor is transient or can be relieved, the symptoms must begin to diminish after not more than 8 hours. If exposure to the stressor continues, the symptoms must begin to diminish after not more than 48 hours.
- E. *Most commonly used exclusion clause.* The reaction must occur in the absence of any other concurrent mental or behavioral disorder in ICD-10 (except generalized anxiety disorder and personality disorders) and not within 3 months of the end of an episode of any other mental or behavioral disorder.

Posttraumatic stress disorder

- A. The patient must have been exposed to a stressful event or situation (either short- or long-lasting) of an exceptionally threatening or catastrophic nature, which would be likely to cause pervasive distress in almost anyone.
- B. There must be persistent remembering or "reliving" of the stressor in intrusive "flashbacks," vivid memories, or recurring dreams or in experiencing distress when exposed to circumstances resembling or associated with the stressor.
- C. The patient must exhibit an actual or preferred avoidance of circumstances resembling or associated with the stressor, which was not present before exposure to the stressor.
- D. Either of the following must be present:
(1) inability to recall, either partially or completely, some important aspects of the period of exposure to the stressor;
(2) persistent symptoms of increased psychological sensitivity and arousal (not present before exposure to the stressor), shown by any two of the following:
(a) difficulty in falling or staying asleep;
(b) irritability or outbursts of anger;
(c) difficulty in concentrating;
(d) hypervigilance;
(e) exaggerated startle response.
- E. Criteria B, C, and D must all be met within 6 months of the stressful event or of the end of a period of stress. (For some purposes, onset delayed more than 6 months may be included, but this should be clearly specified.)

(From World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders: Diagnostic Criteria for Research*. Copyright, World Health Organization, Geneva, 1993, with permission.)

as common, especially in less-severe varieties of these disorders, and a category for cases that cannot be based on a single main syndrome is provided. Although the idea of neurosis is no longer the organizing principle, "care has been taken to allow the easy identification of disorders that some users still might wish to regard as neurotic in their own usage of the term."

The main ICD-10 categories for "neurotic" anxiety disorders are phobic anxiety disorders (agoraphobia, social phobias, and specific phobias); other anxiety disorders (panic disorder, generalized anxiety disorder, and mixed anxiety and depressive disorder); and OCD (with predominantly obsessional thoughts, predominantly compulsive acts, or mixed obsessional thoughts and acts) (Tables 16.1–3 through 16.1–5).

In ICD-10, reaction to severe stress and adjustment disorders are grouped into one category, which is classed together with neurotic and somatoform disorders. The stress-related category differs from the other two categories, however, because it can be defined on the basis of both symptoms and one of two causative influences: a stressful life event causing an acute stress reaction or a significant life change producing an adjustment disorder. Stress-related disorders in all age groups, including children, fall into this category.

In this group, ICD-10 classifies reactions to severe stress (acute stress reaction, posttraumatic distress disorder) and adjustment disorders (see Chapter 26). ICD-10 also includes the dissociative (conversion) disorders in the category of stress-related disorders. (For a discussion of dissociative disorders, see Chapter 20.) The criteria for reactions to severe stress are given in Table 16.1–6.

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▲ 16.2 Panic Disorder and Agoraphobia

An acute intense attack of anxiety accompanied by feelings of impending doom is known as *panic disorder*. The anxiety is characterized by discrete periods of intense fear that can vary from several attacks during one day to only a few attacks during a year. Patients with panic disorder present with a number of comorbid conditions, most commonly agoraphobia, which refers to a fear of or anxiety regarding places from which escape might be difficult.

childhood and a history of separation anxiety. Being alone in public places revives the childhood anxiety about being abandoned. The defense mechanisms used include repression, displacement, avoidance, and symbolization. Traumatic separations during childhood can affect children's developing nervous systems in such a manner that they become susceptible to anxieties in adulthood. A predisposing neurophysiological vulnerability may interact with certain kinds of environmental stressors to produce the resulting panic attack.

Many patients describe panic attacks as coming out of the blue, as though no psychological factors were involved, but psychodynamic exploration frequently reveals a clear psychological trigger for the panic attack. Although panic attacks are correlated neurophysiologically with the locus ceruleus, the onset of panic is generally related to environmental or psychological factors. Patients with panic disorder have a higher incidence of stressful life events (particularly loss) than control subjects in the months before the onset of panic disorder. Moreover, the patients typically experience greater distress about life events than control subjects do.

The hypothesis that stressful psychological events produce neurophysiological changes in panic disorder is supported by a study of female twins. The research findings revealed that panic disorder was strongly associated with both parental separation and parental death before children reached the age of 10. They were approximately seven- and fourfold times, respectively, more likely to be diagnosed with panic disorder with agoraphobia. Separation from the mother early in life was clearly more likely to result in panic disorder than was paternal separation in the cohort of 1,018 pairs of female twins. Another etiological factor in adult female patients appears to be childhood physical and sexual abuse. Approximately 60 percent of women with panic disorder have a history of childhood sexual abuse, compared with 31 percent of women with other anxiety disorders. Further support for psychological mechanisms in panic disorder can be inferred from a study of panic disorder in which patients received successful treatment with cognitive therapy. Before the therapy, the patients responded to panic attack induction with lactate. After successful cognitive therapy, lactate infusion no longer produced a panic attack.

The research indicates that the cause of panic attacks is likely to involve the unconscious meaning of stressful events and that the pathogenesis of the panic attacks may be related to neurophysiological factors triggered by the psychological reactions. Psychodynamic clinicians should always thoroughly investigate possible triggers whenever assessing a patient with panic disorder. The psychodynamics of panic disorder are summarized in Table 16.2-1.

DIAGNOSIS

Panic Attacks

The criteria for a panic attack are listed separately in the DSM-IV-TR (Table 16.2-2). Panic attacks can occur in mental disorders other than panic disorder, particularly in specific phobia, social phobia, and PTSD. Unexpected panic attacks occur at any time and are not associated with any identifiable situational stimulus, but panic attacks need not be unexpected. Attacks in patients with social and specific phobias are usually expected or cued to



Table 16.2-1

Psychodynamic Themes in Panic Disorder

1. Difficulty tolerating anger
2. Physical or emotional separation from significant person both in childhood and in adult life
3. May be triggered by situations of increased work responsibilities
4. Perception of parents as controlling, frightening, critical, and demanding
5. Internal representations of relationships involving sexual or physical abuse
6. A chronic sense of feeling trapped
7. Vicious cycle of anger at parental rejecting behavior followed by anxiety that the fantasy will destroy the tie to parents
8. Failure of signal anxiety function in ego related to self-fragmentation and self-other boundary confusion
9. Typical defense mechanisms: reaction formation, undoing, somatization, and externalization

a recognized or specific stimulus. Some panic attacks do not fit easily into the distinction between unexpected and expected, and these attacks are referred to as *situationally predisposed panic attacks*. They may or may not occur when a patient is exposed to a specific trigger, or they may occur either immediately after exposure or after a considerable delay.

Panic Disorder

The DSM-IV-TR contains two diagnostic criteria for panic disorder, one without agoraphobia (Table 16.2-3) and the other with agoraphobia (Table 16.2-4), but both require the presence of panic attacks as described in Table 16.2-2. Some community surveys have indicated that panic attacks are common, and a major issue in developing diagnostic criteria for panic disorder was determining a threshold number or frequency of panic attacks required to meet the diagnosis. Setting the threshold too



Table 16.2-2

DSM-IV-TR Criteria for Panic Attack

Note: A panic attack is not a codable disorder. Code the specific diagnosis in which the panic attack occurs (e.g., panic disorder with agoraphobia).

A discrete period of intense fear or discomfort, in which four (or more) of the following symptoms developed abruptly and reached a peak within 10 minutes:

- (1) palpitations, pounding heart, or accelerated heart rate
- (2) sweating
- (3) trembling or shaking
- (4) sensations of shortness of breath or smothering
- (5) feeling of choking
- (6) chest pain or discomfort
- (7) nausea or abdominal distress
- (8) feeling dizzy, unsteady, lightheaded, or faint
- (9) derealization (feelings of unreality) or depersonalization (being detached from oneself)
- (10) fear of losing control or going crazy
- (11) fear of dying
- (12) paresthesias (numbness or tingling sensations)
- (13) chills or hot flushes

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Table 16.2-3
DSM-IV-TR Diagnostic Criteria for Panic Disorder without Agoraphobia

- A. Both (1) and (2):
 (1) recurrent unexpected panic attacks
 (2) at least one of the attacks has been followed by 1 month (or more) of one (or more) of the following:
 (a) persistent concern about having additional attacks
 (b) worry about the implications of the attack or its consequences (e.g., losing control, having a heart attack, "going crazy")
 (c) a significant change in behavior related to the attacks
- B. Absence of agoraphobia
- C. The panic attacks are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hyperthyroidism).
- D. The panic attacks are not better accounted for by another mental disorder, such as social phobia (e.g., occurring on exposure to feared social situations), specific phobia (e.g., on exposure to a specific phobic situation), obsessive-compulsive disorder (e.g., on exposure to dirt in someone with an obsession about contamination), posttraumatic stress disorder (e.g., in response to stimuli associated with a severe stressor), or separation anxiety disorder (e.g., in response to being away from home or close relatives).

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low results in the diagnosis of panic disorder in patients who do not have an impairment from an occasional panic attack; setting the threshold too high results in a situation in which patients who are impaired by their panic attacks do not meet the diagnostic criteria. The vagaries of setting a threshold are evidenced



Table 16.2-4
DSM-IV-TR Diagnostic Criteria for Panic Disorder with Agoraphobia

- A. Both (1) and (2):
 (1) recurrent unexpected panic attacks
 (2) at least one of the attacks has been followed by 1 month (or more) of one (or more) of the following:
 (a) persistent concern about having additional attacks
 (b) worry about the implications of the attack or its consequences (e.g., losing control, having a heart attack, "going crazy")
 (c) a significant change in behavior related to the attacks
- B. The presence of agoraphobia
- C. The panic attacks are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hyperthyroidism).
- D. The panic attacks are not better accounted for by another mental disorder, such as social phobia (e.g., occurring on exposure to feared social situations), specific phobia (e.g., on exposure to a specific phobic situation), obsessive-compulsive disorder (e.g., on exposure to dirt in someone with an obsession about contamination), posttraumatic stress disorder (e.g., in response to stimuli associated with a severe stressor), or separation anxiety disorder (e.g., in response to being away from home or close relatives).

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by the range of thresholds set in various diagnostic criteria. The Research Diagnostic Criteria require six panic attacks during a 6-week period. The 10th revision of the *International Statistical Classification of Diseases and Related Health Problems* (ICD-10) requires three attacks in 3 weeks (for moderate disease) or four attacks in 4 weeks (for severe disease). DSM-IV-TR does not specify a minimal number of panic attacks or a time frame but does require that at least one attack be followed by at least a month-long period of concern about having another panic attack or about the implications of the attack or a significant change in behavior. DSM-IV-TR also requires that the panic attacks generally be unexpected, but allows for expected or situationally predisposed attacks.

Agoraphobia without History of Panic Disorder

Table 16.2-5 lists criteria for agoraphobia. The DSM-IV-TR diagnostic criteria for agoraphobia without history of panic disorder (Table 16.2-6) are based on the fear of a sudden incapacitating or embarrassing symptom. In contrast, the ICD-10 criteria require the presence of interrelated or overlapping phobias, but do not require fear of incapacitating or embarrassing symptoms.

The DSM-IV-TR criteria also address the avoidance of situations that are based on a concern related to a medical disorder (e.g., fear of a myocardial infarction in a patient with severe heart disease).



Table 16.2-5
DSM-IV-TR Criteria for Agoraphobia

Note: Agoraphobia is not a codable disorder. Code the specific disorder in which the agoraphobia occurs (e.g., panic disorder with agoraphobia or agoraphobia without history of panic disorder).

- A. Anxiety about being in places or situations from which escape might be difficult (or embarrassing) or in which help may not be available in the event of having an unexpected or situationally predisposed panic attack or panic-like symptoms. Agoraphobic fears typically involve characteristic clusters of situations that include being outside the home alone; being in a crowd or standing in a line; being on a bridge; and traveling in a bus, train, or automobile.
Note: Consider the diagnosis of specific phobia if the avoidance is limited to one or only a few specific situations, or social phobia if the avoidance is limited to social situations.
- B. The situations are avoided (e.g., travel is restricted) or else are endured with marked distress or with anxiety about having a panic attack or panic-like symptoms, or require the presence of a companion.
- C. The anxiety or phobic avoidance is not better accounted for by another mental disorder, such as social phobia (e.g., avoidance limited to social situations because of fear of embarrassment), specific phobia (e.g., avoidance limited to a single situation like elevators), obsessive-compulsive disorder (e.g., avoidance of dirt in someone with an obsession about contamination), posttraumatic stress disorder (e.g., avoidance of stimuli associated with a severe stressor), or separation anxiety disorder (e.g., avoidance of leaving home or relatives).

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comorbid with major depression: Factors mediating the association with suicidal behavior. *Am J Psychiatry*. 2005;162:560-566.

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▲ 16.6 Generalized Anxiety Disorder

Anxiety can be conceptualized as a normal and adaptive response to threat that prepares the organism for flight or fight. Persons who seem to be anxious about almost everything, however, are likely to be classified as having generalized anxiety disorder. The text revision of the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR)* defines generalized anxiety disorder as excessive anxiety and worry about several events or activities for most days during at least a 6-month period. The worry is difficult to control and is associated with somatic symptoms, such as muscle tension, irritability, difficulty sleeping, and restlessness. The anxiety is not focused on features of another Axis I disorder, is not caused by substance use or a general medical condition, and does not occur only during a mood or psychiatric disorder. The anxiety is difficult to control, is subjectively distressing, and produces impairment in important areas of a person's life.

EPIDEMIOLOGY

Generalized anxiety disorder is a common condition; reasonable estimates for its 1-year prevalence range from 3 to 8 percent. The ratio of women to men with the disorder is about 2 to 1, but the ratio of women to men who are receiving inpatient treatment for the disorder is about 1 to 1. A lifetime prevalence is close to 5 percent with the Epidemiological Catchment Area (ECA) study suggesting a lifetime prevalence as high as 8 percent. In anxiety disorder clinics about 25 percent of patients have generalized anxiety disorder. The disorder usually has its onset in late adolescence or early adulthood, although cases are commonly seen in older adults. Also, some evidence suggests that the prevalence of generalized anxiety disorder is particularly high in primary care settings.

COMORBIDITY

Generalized anxiety disorder is probably the disorder that most often coexists with another mental disorder, usually social phobia, specific phobia, panic disorder, or a depressive disorder. Perhaps 50 to 90 percent of patients with generalized anxiety disorder have another mental disorder. As many as 25 percent of patients eventually experience panic disorder. Generalized anxiety disorder is differentiated from panic disorder by the absence of spontaneous panic attacks. An additional high percentage of patients are likely to have major depressive disorder. Other common

disorders associated with generalized anxiety disorder are dysthymic disorder and substance-related disorders.

ETIOLOGY

The cause of generalized anxiety disorder is not known. As currently defined, generalized anxiety disorder probably affects a heterogeneous group of persons. Perhaps because a certain degree of anxiety is normal and adaptive, differentiating normal anxiety from pathological anxiety and differentiating biological causative factors from psychosocial factors are difficult. Biological and psychological factors probably work together.

Biological Factors

The therapeutic efficacies of benzodiazepines and the azaspirones (e.g., buspirone [BuSpar]) have focused biological research efforts on the γ -aminobutyric acid and serotonin neurotransmitter systems. Benzodiazepines (which are benzodiazepine receptor agonists) are known to reduce anxiety, whereas flumazenil (Romazicon) (a benzodiazepine receptor antagonist) and the β -carbolines (benzodiazepine receptor reverse agonists) are known to induce anxiety. Although no convincing data indicate that the benzodiazepine receptors are abnormal in patients with generalized anxiety disorder, some researchers have focused on the occipital lobe, which has the highest concentrations of benzodiazepine receptors in the brain. Other brain areas hypothesized to be involved in generalized anxiety disorder are the basal ganglia, the limbic system, and the frontal cortex. Because buspirone is an agonist at the serotonin 5-HT_{1A} receptor, there is the hypothesis that the regulation of the serotonergic system in generalized anxiety disorder is abnormal. Other neurotransmitter systems that have been the subject of research in generalized anxiety disorder include the norepinephrine, glutamate, and cholecystokinin systems. Some evidence indicates that patients with generalized anxiety disorder may have subsensitivity of their α_2 -adrenergic receptors, as indicated by a blunted release of growth hormone after clonidine (Catapres) infusion.

Brain-imaging studies of patients with generalized anxiety disorder have revealed significant findings. One positron emission tomography study reported a lower metabolic rate in basal ganglia and white matter in patients with generalized anxiety disorder than in normal control subjects (Fig. 16.6-1). A few genetic studies have also been conducted in the field. One study found that a genetic relation might exist between generalized anxiety disorder and major depressive disorder in women. Another study showed a distinct, but difficult-to-quantitate, genetic component in generalized anxiety disorder. About 25 percent of first-degree relatives of patients with generalized anxiety disorder are also affected. Male relatives are likely to have an alcohol use disorder. Some twin studies report a concordance rate of 50 percent in monozygotic twins and 15 percent in dizygotic twins. Table 16.6-1 lists relative genetic risks in selected anxiety disorders.

A variety of electroencephalogram (EEG) abnormalities has been noted in alpha rhythm and evoked potentials. Sleep EEG studies have reported increased sleep discontinuity, decreased delta sleep, decreased stage 1 sleep, and reduced rapid eye movement sleep. These changes in sleep architecture differ from the changes seen in depressive disorders.

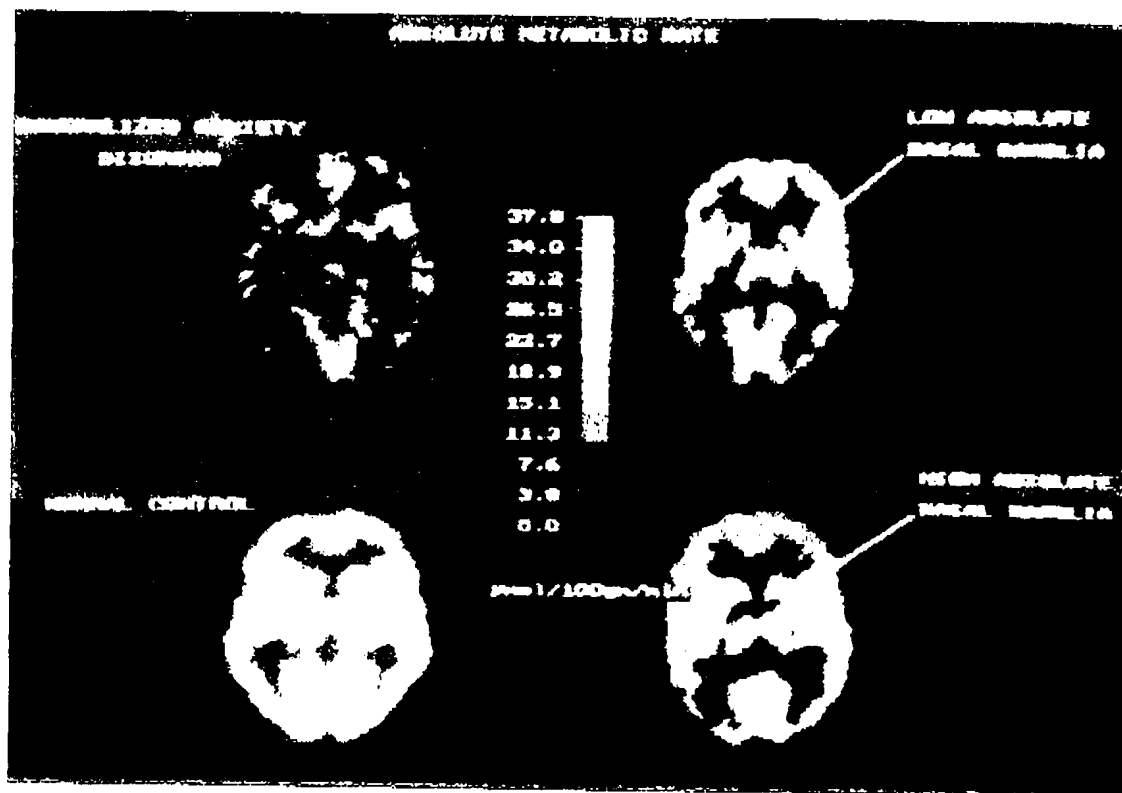


FIGURE 16.6-1

Basal ganglia metabolism. A common glucose scale shows the decrease in absolute glucose metabolic rate in the basal ganglia of two typical subjects with generalized anxiety disorder (**top row**) compared with two normal control subjects (**bottom row**). (From Wu JC, Buchsbaum MS, Hershey TG, Hazlett E, Sicotte N, Johnson JC. PET in generalized anxiety disorder. *Biol Psychiatry* 1991;29:1188, with permission.)

Psychosocial Factors

The two major schools of thought about psychosocial factors leading to the development of generalized anxiety disorder are the cognitive-behavioral school and the psychoanalytic school. According to the cognitive-behavioral school, patients with generalized anxiety disorder respond to incorrectly and inaccurately perceived dangers. The inaccuracy is generated by selective attention to negative details in the environment, by distortions in information processing, and by an overly negative view of the person's own ability to cope. The psychoanalytic school hypothesizes that anxiety is a symptom of unresolved, unconscious conflicts. Sigmund Freud first presented this psychological theory in 1909 with his description of Little Hans; before then, Freud had conceptualized anxiety as having a physiological basis. An

example of Freudian theory as applied to general anxiety can be seen in the following case:

Mrs. B, a 26-year-old married woman, was admitted to the hospital for the evaluation of persistent anxiety that had begun 8 months earlier and was becoming increasingly disabling. Especially disturbing to the patient was the spontaneous intrusion of intermittent images in her mind's eye of her father and herself locked in a naked sexual embrace. The images were not only frightening, but they puzzled her greatly, for she had always disliked her father intensely. Not only was he "poison" to her, but she tried to avoid any contact with him and found it difficult to talk to him if she was forced to be in his company.

As the patient described the difficulty of her relationship with her father, she suddenly recalled that her anxiety had begun at a time when her father was seemingly being more intrusive than ever as he tried to help her and her husband over a period of financial difficulty.

As the patient continued to revile her father, she suddenly commented that her mother had told her that her father "had been good to me when I was little and he used to sing songs to me and take me on his lap, but I don't remember. I only remember when he was mean to me. I just am glad when he keeps on talking mean to me the way he always has. I just wouldn't know what to do if he was nice to me." When asked by the interviewer if there might have been a time when she had wanted him to be nice to her, the patient replied, "When I was little, I just wanted to know that he did love me a little. I guess I always wanted him to be nice to me. But when I stop to think about it, I guess I didn't want him to be nice to me." The doctor then



Table 16.6-1
Familial Relative Risks in Selected
Anxiety Disorders

Disorder	Population Prevalence (%)	Familial Relative Risk ^a
Panic disorder	1-3	2-20
Generalized anxiety disorder	3-5	6
Obsessive-compulsive disorder	1-3	3-5

^aRatio of risk to relatives of cases versus risk to relatives of controls

commented, "It sounds as if a part of you wants to be close to your father." In response, the patient burst into agitated sobs and blurted out, "I don't know how to be close to my father! I am too old to care about my father now!"

When the patient regained her composure, she recalled the memory of an event she had not thought of since it had occurred 15 years earlier. When she was 11, she reported, while in the living room with her father, she had suddenly had the mental image of being in a sexual embrace with him. Terrified, she had run into the kitchen to find her mother. There had been no recurrence of that image until the onset of the current illness, and the incident had remained forgotten until its recall during the interview. Its emergence into consciousness amplified the history of the patient's illness and disclosed an earlier transient outbreak of the same symptoms she had experienced as an adult. After the patient had recovered her composure, she recalled further hitherto forgotten memories. She had slept in her parents' bedroom until she was 6, during which period her father, on one occasion, had taken her into bed and told her stories and, on another, had yelled at her very angrily as she lay in her crib.

During a clinical interview the next day, the patient revealed a fact that she had forgotten in her earlier account of her illness: At the end of the period during which her father had been making the friendly overtures that had so deeply troubled her, and the night before the sudden onset of her symptoms, she had had a nightmare. She was, she dreamed, at a zoo. It was night, and she heard strange noises in the darkness. She asked an attendant standing next to her what the noises were. "Oh," the attendant replied casually, "that's only the animals mating." She then noticed a large, gray elephant lying on its right side in the grass in front of her. As she watched, she noticed the creature moving its left hind leg up and down as if it were trying to get to its feet. At that point she awoke from the dream with a feeling of terror and, afterward, during the morning, experienced the first episode of the frightening imagery of sexual activity with her father.

In direct association to the dream, the patient recalled a long-forgotten childhood memory of an incident that had occurred during her fourth or fifth year. She had awoken one night while in her crib in her parents' bedroom to observe her parents having sexual intercourse. They suddenly became aware of her watching them and sprang apart. The patient remembered seeing her mother hastily pulling up the bedclothes around her to cover her nakedness. Her father, meanwhile, rolled over half on his back, half on his left side. The patient noticed his erection and then saw him lift up his left leg as he sat up and yelled at her angrily to go to sleep.

It was not easy for the patient to communicate these memories. She spoke haltingly, in a low voice and was visibly ashamed and anxious throughout the whole recital of the dream and its associations. She discharged a great quantity of affect, but after doing so, appeared considerably relaxed, relieved, and composed. On her return to the psychiatric ward, she was observed to be cheerful and outgoing with the ward personnel and other patients. Of particular note was that she no longer experienced any anxiety and had no recurrence of the sexual images involving her father that had previously been so deeply distressing. The patient was discharged a short while later after a further series of psychotherapeutic interviews, and when seen for a follow-up visit 2 months later, she reported continued emotional calm and comfort, without recurrence of psychiatric symptoms.

Generalized anxiety disorder, according to DSM-IV-TR, is characterized by a pattern of frequent, persistent worry and anxiety that is out of proportion to the impact of the event or cir-



Table 16.6-2

DSM-IV-TR Diagnostic Criteria for Generalized Anxiety Disorder

- A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance).
- B. The person finds it difficult to control the worry.
- C. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms present for more days than not for the past 6 months).
 Note: Only one item is required in children.
 - (1) restlessness or feeling keyed up or on edge
 - (2) being easily fatigued
 - (3) difficulty concentrating or mind going blank
 - (4) irritability
 - (5) muscle tension
 - (6) sleep disturbance (difficulty falling or staying asleep, or restless unsatisfying sleep)
- D. The focus of the anxiety and worry is not confined to features of an Axis I disorder, e.g., the anxiety or worry is not about having a panic attack (as in panic disorder), being embarrassed in public (as in social phobia), being contaminated (as in obsessive-compulsive disorder), being away from home or close relatives (as in separation anxiety disorder), gaining weight (as in anorexia nervosa), having multiple physical complaints (as in somatization disorder), or having a serious illness (as in hypochondriasis), and the anxiety and worry do not occur exclusively during posttraumatic stress disorder.
- E. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- F. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hyperthyroidism) and does not occur exclusively during a mood disorder, a psychotic disorder, or a pervasive developmental disorder.

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cumstance that is the focus of the worry (Table 16.6-2). The distinction between generalized anxiety disorder and normal anxiety is emphasized by the use of the words "excessive" and "difficult to control" in the criteria and by the specification that the symptoms cause significant impairment or distress.

CLINICAL FEATURES

The essential characteristics of generalized anxiety disorder are sustained and excessive anxiety and worry accompanied by a number of physiological symptoms, including motor tension, autonomic hyperactivity, and cognitive vigilance (Table 16.6-3). The anxiety is excessive and interferes with other aspects of a person's life. This pattern must occur more days than not for at least 6 months. The motor tension is most commonly manifested as shakiness, restlessness, and headaches. The autonomic hyperactivity is commonly manifested by shortness of breath, excessive sweating, palpitations, and various gastrointestinal symptoms. The cognitive vigilance is evidenced by irritability and the ease with which patients are startled.



Table 16.6–3
Physiological Symptoms of Anxiety Disorders
Explicitly Mentioned in DSM-IV-TR

Panic disorder
Palpitations, pounding heart, or accelerated heart rate
Sweating
Trembling or shaking
Sensation of shortness of breath or smothering
Feeling of choking
Chest pain or discomfort
Nausea or abdominal distress
Feeling dizzy, unsteady, lightheaded, or faint
Chills or hot flushes
Posttraumatic stress disorder
Physiological reactivity on exposure to trauma-related cues
Difficulties falling asleep or staying asleep
Exaggerated startle response
Generalized anxiety disorder
Muscle tension
Sleep disturbance
Acute stress disorder
Marked symptoms of arousal

Patients with generalized anxiety disorder usually seek out a general practitioner or internist for help with a somatic symptom. Alternatively, the patients go to a specialist for a specific symptom (e.g., chronic diarrhea). A specific nonpsychiatric medical disorder is rarely found, and patients vary in their doctor-seeking behavior. Some patients accept a diagnosis of generalized anxiety disorder and the appropriate treatment; others seek additional medical consultations for their problems. Generalized anxiety disorders can be disabling as in the following case.

A 27-year-old married electrician complained of dizziness, sweating palms, heart palpitations, and ringing of the ears of more than 18 months' duration. He also experienced dry mouth and throat, periods of extreme muscle tension, and a constant "edgy" and watchful feeling that had often interfered with his ability to concentrate. These feelings had been present most of the time over the previous 2 years; they had not been limited to discrete periods. Although these symptoms made him feel "discouraged," he denied feeling depressed and continued to enjoy activities with his family.

Because of these symptoms the patient had seen a family practitioner, a neurologist, a neurosurgeon, a chiropractor, and an ear-nose-throat specialist. He had been placed on a hypoglycemic diet, received physiotherapy for a pinched nerve, and been told he might have "an inner ear problem."

He also had many worries. He constantly worried about the health of his parents. His father, in fact, had a myocardial infarction 2 years previously, but is now feeling well. He also worried about whether he is "a good father," whether his wife will ever leave him (there is no indication that she is dissatisfied with the marriage), and whether he is liked by co-workers on the job. Although he recognizes that his worries are often unfounded, he can't stop worrying.

For the past 2 years the patient has had few social contacts because of his nervous symptoms. Although he sometimes had to leave work when the symptoms became intolerable, he continues to work for the same company he joined for his apprenticeship following high-school graduation. He tends to hide his symptoms from his wife and children, to whom he wants to appear "perfect." (Adapted from *DSM-IV-TR Casebook*.)

DIFFERENTIAL DIAGNOSIS

As with other anxiety disorders, generalized anxiety disorder must be differentiated from both medical and psychiatric disorders. Neurological, endocrinological, metabolic, and medication-related disorders similar to those considered in the differential diagnosis of panic disorder must be considered in the differential diagnosis of generalized anxiety disorder. Common co-occurring anxiety disorders also must be considered, including panic disorder, phobias, obsessive-compulsive disorder (OCD), and posttraumatic stress disorder (PTSD). To meet criteria for generalized anxiety disorder, patients must both exhibit the full syndrome and their symptoms also cannot be explained by the presence of a comorbid anxiety disorder. To diagnose generalized anxiety disorder in the context of other anxiety disorders, it is most important to document anxiety or worry related to circumstances or topics that are either unrelated, or only minimally related, to other disorders. Proper diagnosis involves both definitively establishing the presence of generalized anxiety disorder and properly diagnosing other anxiety disorders. Patients with generalized anxiety disorder frequently develop major depressive disorder. As a result, this condition must also be recognized and distinguished. The key to making a correct diagnosis is documenting anxiety or worry that is unrelated to the depressive disorder.

COURSE AND PROGNOSIS

The age of onset is difficult to specify; most patients with the disorder report that they have been anxious for as long as they can remember. Patients usually come to a clinician's attention in their 20s, although the first contact with a clinician can occur at virtually any age. Only one third of patients who have generalized anxiety disorder seek psychiatric treatment. Many go to general practitioners, internists, cardiologists, pulmonary specialists, or gastroenterologists, seeking treatment for the somatic component of the disorder. Because of the high incidence of comorbid mental disorders in patients with generalized anxiety disorder, the clinical course and prognosis of the disorder are difficult to predict. Nonetheless, some data indicate that life events are associated with the onset of generalized anxiety disorder: The occurrence of several negative life events greatly increases the likelihood that the disorder will develop. By definition, generalized anxiety disorder is a chronic condition that may well be lifelong.

TREATMENT

The most effective treatment of generalized anxiety disorder is probably one that combines psychotherapeutic, pharmacotherapeutic, and supportive approaches. The treatment may take a significant amount of time for the involved clinician, whether the clinician is a psychiatrist, a family practitioner, or another specialist.

Psychotherapy

The major psychotherapeutic approaches to generalized anxiety disorder are cognitive-behavioral, supportive, and insight oriented. Data are still limited on the relative merits of those

approaches, although the most sophisticated studies have examined cognitive-behavioral techniques, which seem to have both short-term and long-term efficacy. Cognitive approaches address patients' hypothesized cognitive distortions directly, and behavioral approaches address somatic symptoms directly. The major techniques used in behavioral approaches are relaxation and biofeedback. Some preliminary data indicate that the combination of cognitive and behavioral approaches is more effective than either technique used alone. Supportive therapy offers patients reassurance and comfort, although its long-term efficacy is doubtful. Insight-oriented psychotherapy focuses on uncovering unconscious conflicts and identifying ego strengths. The efficacy of insight-oriented psychotherapy for generalized anxiety disorder is found in many anecdotal case reports, but large controlled studies are lacking.

Most patients experience a marked lessening of anxiety when given the opportunity to discuss their difficulties with a concerned and sympathetic physician. If clinicians discover external situations that are anxiety provoking, they may be able—alone or with the help of the patients or their families—to change the environment and, thus, reduce the stressful pressures. A reduction in symptoms often allows patients to function effectively in their daily work and relationships and, thus, gain new rewards and gratification that are themselves therapeutic.

In the psychoanalytic perspective, anxiety sometimes signals unconscious turmoil that deserves investigation. The anxiety can be normal, adaptive, maladaptive, too intense, or too mild, depending on the circumstances. Anxiety appears in numerous situations over the course of the life cycle; in many cases, symptom relief is not the most appropriate course of action.

For patients who are psychologically minded and motivated to understand the sources of their anxiety, psychotherapy may be the treatment of choice. Psychodynamic therapy proceeds with the assumption that anxiety can increase with effective treatment. The goal of the dynamic approach may be to increase the patient's anxiety tolerance (a capacity to experience anxiety without having to discharge it), rather than to eliminate anxiety. Empirical research indicates that many patients who have successful psychotherapeutic treatment may continue to experience anxiety after termination of the psychotherapy, but their increased ego mastery allows them to use the anxiety symptoms as a signal to reflect on internal struggles and to expand their insight and understanding. A psychodynamic approach to patients with generalized anxiety disorder involves a search for the patient's underlying fears.

Pharmacotherapy

The decision to prescribe an anxiolytic to patients with generalized anxiety disorder should rarely be made on the first visit. Because of the long-term nature of the disorder, a treatment plan must be carefully thought out. The three major drugs to be considered for the treatment of generalized anxiety disorder are benzodiazepines, the serotonin-specific reuptake inhibitors (SSRIs), buspirone (BuSpar), and venlafaxine (Effexor). Other drugs that may be useful are the tricyclic drugs (e.g., imipramine [Tofranil]), antihistamines, and the β -adrenergic antagonists (e.g., propranolol [Inderal]).

Although drug treatment of generalized anxiety disorder is sometimes seen as a 6- to 12-month treatment, some evidence

indicates that treatment should be long term, perhaps lifelong. About 25 percent of patients relapse in the first month after the discontinuation of therapy, and 60 to 80 percent relapse over the course of the next year. Although some patients become dependent on the benzodiazepines, tolerance rarely develops to the therapeutic effects of the benzodiazepines, buspirone, venlafaxine, or the SSRIs.

Benzodiazepines. Benzodiazepines have been the drugs of choice for generalized anxiety disorder. They can be prescribed on an as-needed basis, so that patients take a rapidly acting benzodiazepine when they feel particularly anxious. The alternative approach is to prescribe benzodiazepines for a limited period, during which psychosocial therapeutic approaches are implemented.

Several problems are associated with the use of benzodiazepines in generalized anxiety disorder. About 25 to 30 percent of all patients fail to respond, and tolerance and dependence can occur. Some patients also experience impaired alertness while taking the drugs and, therefore, are at risk for accidents involving automobiles and machinery.

The clinical decision to initiate treatment with a benzodiazepine should be considered and specific. The patient's diagnosis, the specific target symptoms, and the duration of treatment should all be defined, and the information should be shared with the patient. Treatment for most anxiety conditions lasts for 2 to 6 weeks, followed by 1 or 2 weeks of tapering drug use before it is discontinued. The most common clinical mistake with benzodiazepine treatment is routinely to continue treatment indefinitely.

For the treatment of anxiety, it is usual to begin giving a drug at the low end of its therapeutic range and to increase the dosage to achieve a therapeutic response. The use of a benzodiazepine with an intermediate half-life (8 to 15 hours) will likely avoid some of the adverse effects associated with the use of benzodiazepines with long half-lives, and the use of divided doses prevents the development of adverse effects associated with high peak plasma levels. The improvement produced by benzodiazepines may go beyond a simple antianxiety effect. For example, the drugs may cause patients to regard various occurrences in a positive light. The drugs can also have a mild disinhibiting action, similar to that observed after ingesting modest amounts of alcohol.

Buspirone. Buspirone is a 5-HT_{1A} receptor partial agonist and is most likely effective in 60 to 80 percent of patients with generalized anxiety disorder. Data indicate that buspirone is more effective in reducing the cognitive symptoms of generalized anxiety disorder than in reducing the somatic symptoms. Evidence also indicates that patients who have previously had treatment with benzodiazepines are not likely to respond to treatment with buspirone. The lack of response may be caused by the absence, with buspirone treatment, of some of the nonanxiolytic effects of benzodiazepines (e.g., muscle relaxation and the additional sense of well-being). The major disadvantage of buspirone is that its effects take 2 to 3 weeks to become evident, in contrast to the almost immediate anxiolytic effects of the benzodiazepines. One approach is to initiate benzodiazepine and buspirone use simultaneously, then taper off the benzodiazepine use after 2 to 3 weeks, at which point the buspirone should have reached its maximal effects. Some studies have

also reported that long-term combined treatment with benzodiazepine and buspirone may be more effective than either drug alone. Buspirone is not an effective treatment for benzodiazepine withdrawal.

Venlafaxine. Venlafaxine is effective in treating the insomnia, poor concentration, restlessness, irritability, and excessive muscle tension associated with generalized anxiety disorder. Venlafaxine is a nonselective inhibitor of the reuptake of three biogenic amines—serotonin, norepinephrine, and, to a lesser extent, dopamine.

Selective Serotonin Reuptake Inhibitors. SSRIs may be effective, especially for patients with comorbid depression. The prominent disadvantage of SSRIs, especially fluoxetine (Prozac), is that they can transiently increase anxiety and cause agitated states. For this reason, the SSRIs sertraline (Zoloft), citalopram (Celexa), or paroxetine (Paxil) are better choices in patients with high anxiety disorder. It is reasonable to begin treatment with sertraline, citalopram, or paroxetine plus a benzodiazepine, then to taper benzodiazepine use after 2 to 3 weeks. Further studies are needed to determine whether SSRIs are as effective for generalized anxiety disorder as they are for panic disorder and OCD.

Other Drugs. If conventional pharmacological treatment (e.g., with buspirone or a benzodiazepine) is ineffective or not completely effective, then a clinical reassessment is indicated to rule out comorbid conditions, such as depression, or to better understand the patient's environmental stresses. Other drugs that have proved useful for generalized anxiety disorder include the tricyclic and tetracyclic drugs. The β -adrenergic receptor antagonists may reduce the somatic manifestations of anxiety, but not the underlying condition, and their use is usually limited to situational anxieties, such as performance anxiety.

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▲ 16.7 Other Anxiety Disorders

ANXIETY DISORDER DUE TO A GENERAL MEDICAL CONDITION

Many medical disorders are associated with anxiety. Symptoms can include panic attacks, generalized anxiety, obsessions and compulsions, and other signs of distress. In all cases, the signs and symptoms will be due to the direct physiological effects of the medical condition.

Epidemiology

The occurrence of anxiety symptoms related to general medical conditions is common, although the incidence of the disorder varies for each specific general medical condition.

Etiology

A wide range of medical conditions can cause symptoms similar to those of anxiety disorders (Table 16.7–1). Hyperthyroidism (see Color Plate 16.7–1 on page 494), hypothyroidism, hypoparathyroidism, and vitamin B₁₂ deficiency are frequently associated with anxiety symptoms. A pheochromocytoma produces epinephrine, which can cause paroxysmal episodes of anxiety symptoms. Certain lesions of the brain and postencephalitic states reportedly produce symptoms identical to those seen in obsessive-compulsive disorder (OCD). Other medical conditions, such as cardiac arrhythmia, can produce physiological symptoms of panic disorder. Hypoglycemia can also mimic the symptoms of an anxiety disorder. The diverse medical conditions that can cause symptoms of anxiety disorder may do so through a common mechanism, the noradrenergic system, although the effects on the serotonergic system are also under study. Each of these conditions is characterized by prominent anxiety that arises as the direct result of some underlying physiological perturbation.

Diagnosis

The text revision of the fourth edition of *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR) diagnosis of anxiety disorder due to a general medical condition (Table 16.7–2) requires the presence of symptoms of an anxiety disorder. DSM-IV-TR allows clinicians to specify whether the disorder is characterized by symptoms of generalized anxiety, panic attacks, or obsessive-compulsive symptoms.

Clinicians should have an increased level of suspicion for the diagnosis when chronic or paroxysmal anxiety is associated with a physical disease known to cause such symptoms in some patients. Paroxysmal bouts of hypertension in an anxious patient may indicate that a workup for a pheochromocytoma is appropriate. A general medical workup may reveal diabetes, an adrenal tumor, thyroid disease, or a neurological condition. For example, some patients with complex partial epilepsy have extreme